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Characteristics of Radiation-Induced Performance Changes in Bar-Press Avoidance With and Without a Preshock Warning Cue

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BURGHARDT, W. F., JR. AND W. A. HUNT. *Characteristics of radiation-induced performance changes in bar-press avoidance with and without a preshock warning cue.* PHARMACOL BIOCHEM BEHAV **33**(3) 549–554, 1989.—Rats were trained to perform one of three tasks in which responses on a lever delayed the onset of footshock for 20 sec. One task provided a warning tone beginning 15 sec after the last response on the lever and lasting for 5 sec just prior to the presentation of a shock (fixed-interval signalled avoidance), while a second task provided no external cues (unsignalled avoidance). The third task was similar to the fixed-interval signalled avoidance task, except that the warning tone preceding shock began at varying intervals after the last response on the lever (variable-inteval signalled avoidance). Animals trained on the signalled avoidance paradigms received fewer shocks than those on the unsignalled avoidance paradigm. After 10 krads of gamma radiation, animals performing on either task with cues were less able to avoid shock, although they recovered somewhat over a 90-min period. The animals not provided cues also experienced more shocks during the first 10 min after irradiation but were relatively less affected in performing the task. Response rates on the bar and the patterns of responding on these tasks were not significantly different after irradiation, except that animals responded after the onset of shock more often after irradiation than before. These results suggest that rats will continue to effectively use task related cues after irradiation, but that the relative degree of behavioral decrement may depend on the initial level of performance or possibly the complexity of the task.

Performance Ionizing radiation Avoidance Cues

BEHAVIORAL deficits are commonly observed in laboratory animals after high doses of ionizing radiation and have been found as degraded performance on a number of tasks (6). Behavioral abnormalities have been observed in victims of a number of nuclear accidents, including the one at Chernobyl (4, 7, 8). Although some of these responses could have resulted from generalized trauma, they might reflect an effect of ionizing radiation on behavior. This laboratory has been studying the ability of rats to actively avoid shock and how exposure to ionizing radiation can disrupt this behavior. Initial studies involved using a task in which animals learned to jump up onto a ledge to avoid an electrical foot-shock (5). Auditory cues were provided to alert subjects to an impending shock. The results demonstrated that doses of 2.5 to 20 krads of high-energy electrons or gamma photons degraded the performance on this active avoidance task in a dose-dependent manner. Escape behavior was unaltered. Furthermore, electrons were more effective than photons in disrupting this task.

In an attempt to characterize this effect, additional experiments were undertaken to determine whether the animals were capable of performing the required movements and whether they would ask for and use visual and auditory cues to enhance performance (2). A paradigm was used that involved responses on two levers each with different consequences (1). When one lever was pressed, an electrical shock occurring at 5-sec intervals was postponed for 20 sec. Pressing the other lever activated a visual cue (overhead light) for a 60-sec period, during which an auditory cue (tone) occurred 5 sec before the presentation of each shock. The animals rapidly learned to respond for the tone and to use it to effectively avoid shock.

A 10-krad dose of gamma photons severely disrupted the ability of animals to perform this task (2). Almost immediately after irradiation, the animals received significantly more shocks than controls. However, the animals could readily execute the required movements of pressing a bar. In fact, responding on the lever to avoid shock increased, but mostly just subsequent to the onset of shock. In addition, irradiated subjects did not continue to respond to produce the visual and auditory cues. In other words,

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instead of responding for the cues, the animals responded to the shocks. When subjects did use the tones after irradiation, they did so in a way which suggested that they detected the cues and were able to respond to them appropriately. In other experiments, animals were shown to receive increased shocks after doses of radiation as low as 2 krads (unpublished observations).

In the present experiments, we attempted to determine whether the presence of temporal and sensory cues influenced an animal's performance after irradiation. In one experiment, rather than require the animals to specifically respond for preshock warning cues as in the previous study (2), these auditory cues were always available (fixed-interval signalled avoidance). In another experiment, no cues other than temporal ones were available (unsignalled avoidance). A third experiment provided no predictability of the onset of shock based on temporal cues. Instead, the subject received the same average number of preshock warning cues as in the experiments using the fixed-interval signalled avoidance paradigm, except that the time of onset of the warning signal after a response was unpredictable temporally (variable-interval signalled avoidance).

METHOD

Thirty-six male Long Evans (Blue Spruce) rats (300 g) were the experimental subjects. Rats were quarantined on arrival and screened for evidence of disease by serology and histopathology before being released from quarantine. The rats were housed individually in polycarbonate isolator cages (Lab Products, Maywood, NJ) on autoclaved hardwood contact bedding ('Beta Chip' Northeastern Products Corp., Warrensburg, NY) and were provided commerical rodent chow ('Wayne Rodent Blok' Continental Grain Co., Chicago, IL) and acidified water (pH 2.5 using HCl) ad lib. Animal holding rooms were kept at 21 ± 1°C with 50 ± 10% relative humidity on a reversed, 12-hr, light:dark lighting cycle with no twilight.

The apparatus and experimental designs were similar to those previously described (2), except as indicated below. Prior to the first training session, animals were placed in the operant chambers for at least 2 hr to familiarize them with the apparatus. Thereafter, each experimental session lasted 4 hr. The animals then were trained to avoid a 0.5-sec, scrambled, electrical footshock (1.0 mA) by responding on the left lever. Responses on the right lever had no scheduled consequence in this study. A single response postponed the onset of shock by 20 sec. In the absence of responding, shock occurred at 5-sec intervals. Twelve of the rats received a 5-sec warning tone just prior to the scheduled presentation of a shock (fixed-interval signalled avoidance) (9). In this group, the onset of the warning tone always followed the last response on the lever by 15 sec. Another 12 rats received the same preshock warning tones, except that the interval between a response on the lever and the onset of the warning cue before the next scheduled shock varied with equal probability between 0.5 and 120 sec. The mean interval was 15 sec (the same as the interval in the fixed-inteval signalled-avoidance group) making the time of the onset of the warning tone in this group effectively unpredictable (variable-interval signalled avoidance). The last 12 rats were trained similarly, except no warning tones were provided (unsignalled avoidance) (10). Training was complete when the animals could successfully avoid more than 90% of the shocks that could be presented (12/min).

During the warning tone, a response on the lever terminated the warning tone and reset the response to tone interval. Responses made during shock presentation terminated both shock and warning tones and also reset the response to tone interval (response to shock interval in unsignalled avoidance). In the absence of a response in either signalled condition, shock onset followed the onset of the preshock warning tone by 5 sec. If no response was made during the shock, the tone and shock terminated simultaneously 0.5 sec after shock onset.

After training, subjects were habituated to the effects of interrupting the schedule and transporting them for irradiation. After 2 hr of performing the task on which the animals were trained, the session was suspended with the tone and response lever disabled. The animal was placed in a Plexiglas restraining tube, transported to the ^{60}Co facility, and returned without being irradiated. The session then resumed. This procedure was repeated daily until there was less than a 10% difference in the number of shocks received and in the number of responses made during the next hour, compared with those during the hour before removing the animals from the conditioning chambers.

After habituation, each group of animals who learned the fixed-interval signalled avoidance, unsignalled avoidance, or variable-interval signalled avoidance tasks was randomly divided into two subgroups, composed of six animals each. From each group of trained animals, one subgroup was irradiated with a single bilateral dose of 10 krads of gamma radiation from a ^{60}Co source at a rate of 6.6 krads/min. Control subgroups were handled identically, except they were not irradiated. The transport time from the radiation facility to the conditioning chambers was less than 5 min. At the end of the study, all animals were euthanized with a barbiturate overdose (80 mg/kg, IP) within 48 hr after irradiation. All animals were submitted for necropsy and found to be free of concurrent disease.

For radiation dosimetry, paired 50-ml ion chambers were used. Delivered dose was expressed as a ratio of the dose measured in a tissue-equivalent plastic phantom enclosed in a restraining tube to that measured free in air.

For the analysis of data, only the measurements made during the 60 min prior to and the 90 min after irradiation were used, periods when the performance of the animals was most consistent. The data collected were divided into six, 10-min blocks before removal from the apparatus for irradiation, and nine, 10-min blocks postirradiation. For response measures, each postirradiation block was totaled and expressed as the percentage of the mean number of responses for the six, 10-min periods immediately preceding irradiation. Responses from the sham-irradiated animals similarly were recorded. All other measures were presented as totals for each 10-min period. The data were analyzed statistically using multiple factor analyses of variance with repeated measures on one factor (11). Radiation dose (0 or 10 krads) was one factor, and the time after treatment was the repeated factor. The level of significance was 0.05.

RESULTS

Unirradiated animals performed well on both signalled and unsignalled avoidance paradigms. However, performance was better when auditory cues were available. Those animals provided warning tones typically received less than five shocks during a 10-min period (Figs. 1 and 2). However, animals provided no warning tones were less proficient in avoiding shock. They typically received about 8 shocks per 10-min period, $F(3,15) = 4.23$, $p < 0.05$ (Fig. 3).

Irradiated animals experienced an increased number of shocks, although they did not exhibit any gross abnormalities in spontaneous behavior and were able to move about freely. Animals performing either signalled avoidance task received approximately 10 times as many shocks during the first 10 min after irradiation [$F(1,10) = 15.69$, $p < 0.05$, for the fixed-interval signalled avoidance group; $F(1,10) = 8.01$, $p < 0.05$, for the variable-interval

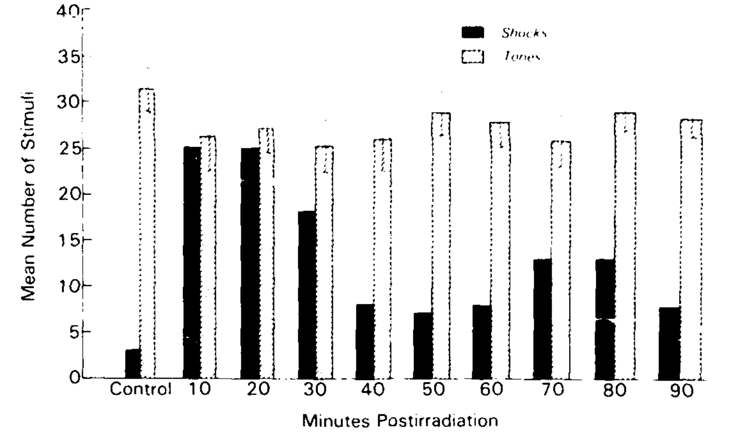

FIG. 1. Mean number of shocks and warning tones, ± SEM, received by animals trained on the fixed-interval signalled avoidance paradigm. Control values are the result of pooling the values for all subjects in the control group for the 90 min after sham irradiation. The data presented were based on observations from 6 animals.

signalled avoidance group], compared to a 2.5-fold increase in shocks received by the animals performing the unsignalled avoidance paradigm, $F(1,10)=0.025$, $p>0.05$. During the remaining 80 min of the session, performance improved, but the number of shocks received by animals performing the two signalled avoidance paradigms continued at a significantly higher level relative to controls. The number of warning tones provided to the animals performing on the signalled avoidance paradigms was unchanged after irradiation [$F(1,10)=2.08$, $p>0.05$, for the fixed-interval signalled avoidance group; $F(1,10)=0.755$, $p>0.05$, for the variable-interval signalled avoidance group] (Figs. 1 and 2).

Although the animal performing on any of the three paradigms experienced more shocks after irradiation, they were still able to respond on the avoidance lever. The response rates varied depending on the paradigm used. With the fixed-interval signalled avoidance paradigm the rate was lowest (63.8 ± 4.7 responses/10-min interval), while that for the unsignalled avoidance paradigm was the highest (103.1 ± 7.2 responses/10-min inteval). The response rate for the variable-interval signalled avoidance group was intermediate (99.4 ± 1.4 responses/10-min interval). However, after irradiation, the average number of responses during each 10-min interval was not significantly different from controls (data not shown).

Since the rate of responding remained unchanged but the number of shocks received increased, the pattern of responding may be altered by irradiation. To test this possibility, interresponse time (IRT) histograms were constructed for the fixed-interval signalled and unsignalled avoidance groups in order to determine the distribution of responses during a session. (The data for the variable-interval signalled avoidance group were not suitable for

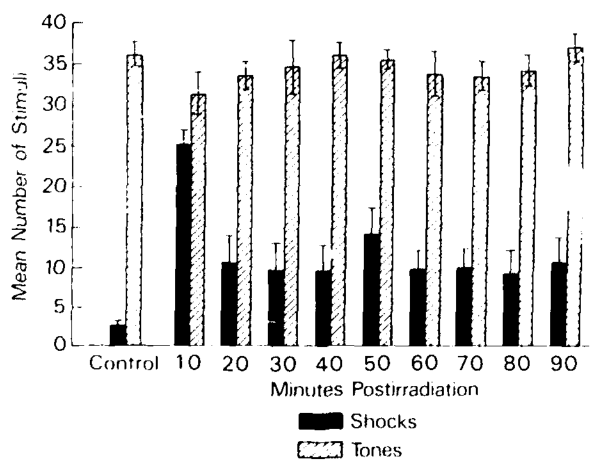

FIG. 2. Mean number of shocks and warning tones, ± SEM, received by animals trained on the variable-interval signalled avoidance paradigm. Control values are the result of pooling the values for all subjects in the control group for the 90 min after sham irradiation. The data presented were based on observations from 6 animals.

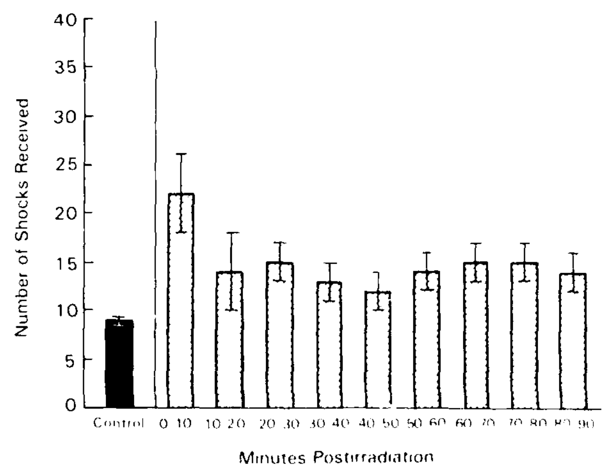

FIG. 3. Mean number of shocks, ± SEM, received by animals trained on the unsignalled avoidance paradigm. Control values are the result of pooling the values of all subjects in the control group for the 90 min after sham irradiation. The data presented were based on observations from 6 animals.

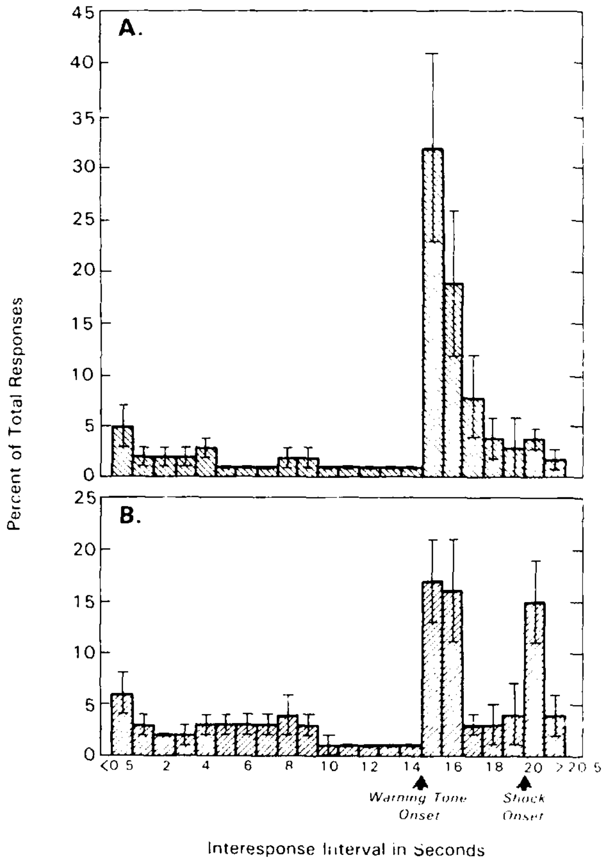

FIG. 4. (A) Interresponse distribution, ± SEM, for the control group trained on the fixed-interval signalled avoidance paradigm after sham irradiation. Arrows indicate the times of onset of warning tones and shocks. (B) Interresponse distribution, ± SEM, for the irradiated group. Scales for both graphs are identical. The mean number of responses per session was 588 ± 46. The data presented were based on observations from 6 animals.

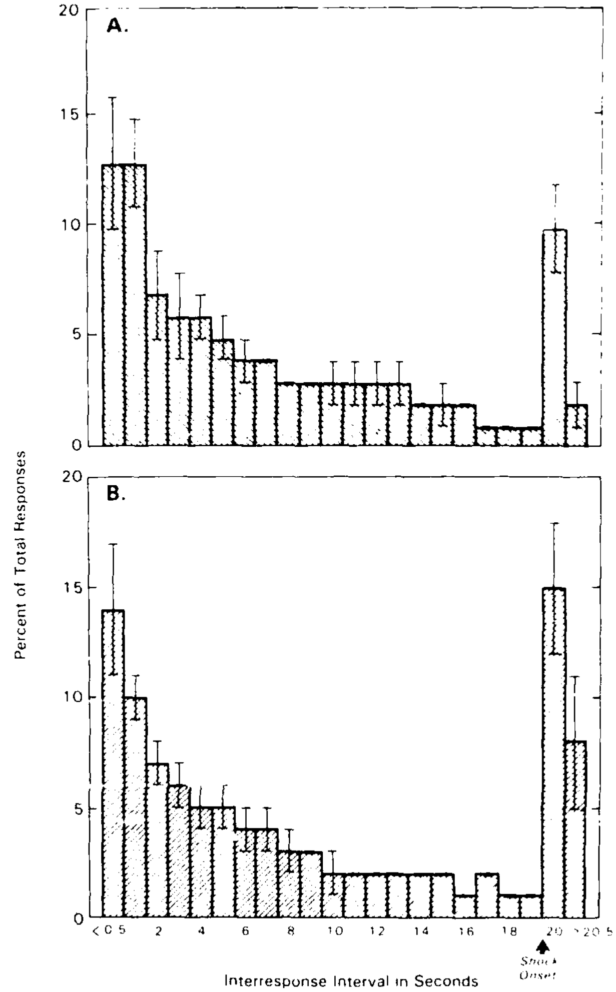

FIG. 5. (A) Interresponse distribution, ± SEM, for the control group trained on the unsignalled avoidance paradigm after sham irradiation. Arrow indicates the time of onset of shocks. (B) Interresponse distribution, ± SEM, for the irradiated group. Scales for both graphs are identical. The mean number of responses per session was 989 ± 84. The data presented were based on observations from 6 animals.

this type of analysis because the animal's response to the warning tone was not reliably related to the subject's last response and consequently showed a flat distribution.) Based on the requirements of the fixed-interval signalled avoidance paradigm, the subjects, as expected, responded mostly just after the onset of the warning tone (Fig. 4A). On the other hand, the animals performing on the unsignalled avoidance paradigm often responded to the shock and continued responding for a time with short IRTs (Fig. 5A). As the IRTs lengthened, a shock eventually occurred, precipitating another period of responses with short IRTs.

The pattern of IRTs after irradiation was not greatly affected. Those animals trained on the fixed-interval signalled avoidance paradigm still responded after the warning tone (Fig. 4B). However, when subjects did not avoid shock, they usually responded just after the onset of shock. Few responses occurred at long intervals after shock. The IRTs of the irradiated animals trained on the unsignalled avoidance paradigm were essentially the same as their corresponding controls, except there were more shock-elicited responses (Fig. 5B).

In order to determine whether the irradiated animals in the fixed-interval signalled avoidance group were really using the warning tones, the latencies between the presentation of the tone and responding on the avoidance lever were determined and are shown in Fig. 6. It was assumed that consistently short latencies to respond would follow the presentation of a tone. Short latencies were found in both irradiated and unirradiated animals, indicating that the animals could detect and use the tones even after irradiation.

Subjects in the variable-interval signalled avoidance group performed similarly to those in the fixed-interval signalled-avoidance group (Fig. 7). The former group also responded with consistently short latencies to the onset of the warning tones in both irradiated and unirradiated conditions, indicating that even when the onset of the warning tone was made unpredictable, the animals continued to wait for it and use it as an aid in responding.

DISCUSSION

The results from this study demonstrate again that exposure to

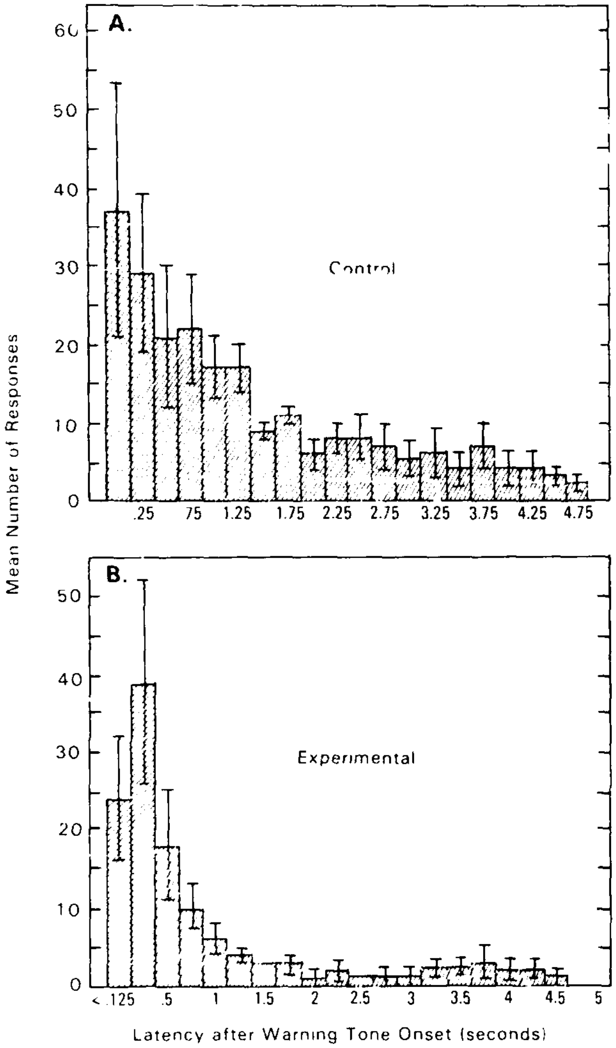

FIG. 6. (A) Latency distribution of responses, ± SEM, to the onset of the warning tone for the animals trained on the fixed-interval signalled avoidance paradigm of the control group during the 90 min after sham irradiation. (B) Latency distribution of responses, ± SEM, to the onset of the warning tone during the 90 min after irradiation. The data presented were based on observations from 6 animals.

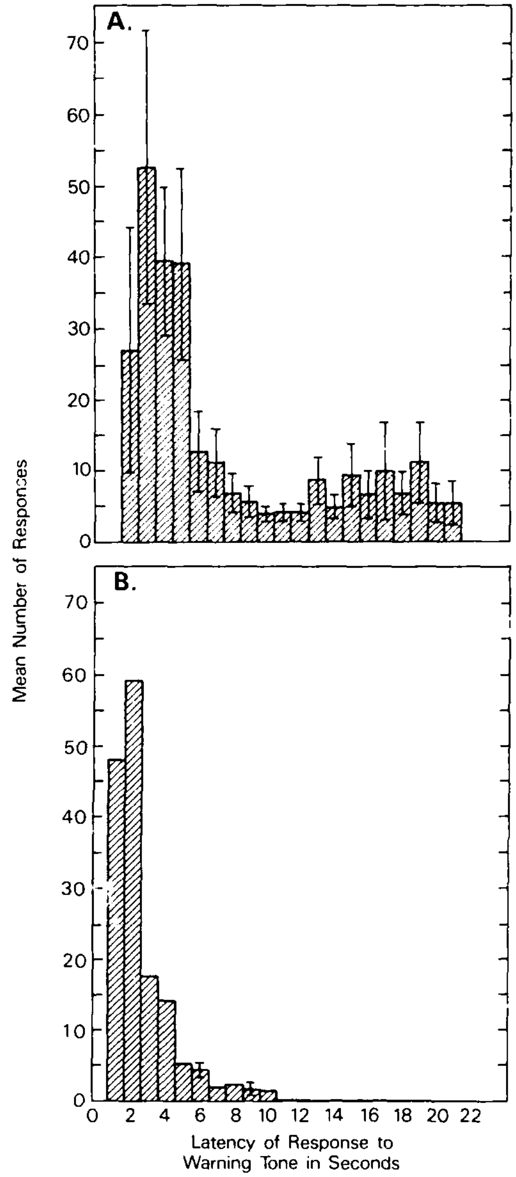

FIG. 7. (A) Latency distribution of responses, ± SEM, to the onset of the warning tone for the animals trained on the variable-interval signalled avoidance paradigm of the control group during the 90 min after sham irradiation. (B) Latency distribution of responses, ± SEM, to the onset of the warning tone during the 90 min after irradiation. Note: In some cases the SEM was too low to be graphed. The data presented were based on observations from 6 animals.

ionizing radiation can degrade performance on active avoidance paradigms and is consistent with previously published reports (2,5). Typically, irradiated animals received more shocks than the unirradiated controls. Although performance was degraded, the animals were capable of executing the movements necessary to avoid shock. The rates and patterns of responding on the avoidance lever were generally unaltered after irradiation, except that animals performing on the two signalled avoidance paradigms responded more frequently to the shock rather than to the warning tone. Even so, it appears that subjects could detect the tones and were able to respond to them appropriately, even when the tones were temporally unpredictable.

The relative degree of behavioral decrement after irradiation appears to depend on the availability of visual and auditory cues that could be used to successfully avoid shocks. Although it can be seen from Figs. 1–3 that the number of shocks received by irradiated animals performing on the three paradigms was roughly the same, the preirradiated levels of performance were different. Prior to irradiation, animals trained on either signalled avoidance paradigm performed significantly better than those animals trained on the unsignalled avoidance paradigm, as evidenced by the fewer number of shocks received by the former animals. These findings suggest that the number and nature of cues and the consequent level of performance (presumably better with cues) have some

bearing on the likelihood of the occurrence of a radiation-induced performance decrement.

Although not the intention of the experimental design, another way to look at the relationship between cues and performance is to consider the three paradigms as requiring of the animals different levels of performance. In order for the animals trained on the two signalled avoidance paradigms to perform as well as they did, compared to those trained on the unsignalled avoidance paradigm, they needed cues to assist them. When the animals were irradiated, for some reason they did not use as many of the cues provided. Consequently, their performance was more like that of irradiated animals trained on the unsignalled avoidance paradigm in which no external cues were provided.

Why the irradiated animals were not using the cues is not clear. They apparently could detect them because responses with short latencies were still observed after presentations of the warning tones before the onset of shock even when the onset of these warning tones was unpredictable. The response pattern is not suggestive of deafness nor stupor, and the subjects were apparently not relying more on internally based time-cues rather than the tones. Another possibility is that they could maintain only temporary selective attention, rather than a more general vigilance. In addition, irradiated rats from other experiments showed no differences in their abilities to detect and respond to warm water cues (3). Rather than these performance decrements being related to abnormalities in perception, task learning, and motor function, they may result from some cognitive deficit, possibly a lack of motivation. That is, the cues and responding to these cues might become of lower value to the subject relative to other cues and behaviors.

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